The domination of knowledge by ignorance: politics and regulation of animal research for diagnosis and treatment of disease

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DR. MARY PUTNAM JACOBI began her short and direct commentary at a hearing in the United States Senate on February 21, 1900: "I will speak . . . the fundamental vice of the bill . . . that is its provisions are deliberately planned for the domination of knowledge by ignorance." She was one of nearly a dozen distinguished leaders of American medicine organized to testify against a bill to regulate (and curtail) animal experimentation in the District of Columbia. The legislation, originally written by the Washington Humane Society, was modeled on the Cruelty to Animals Act passed by Parliament in 1876. The U.S. bill, like the English act, contained provisions for licensing experimentors and their laboratories, restricted the kinds of experiments that could be done by procedure and species, called for inspectors (originally specified as members of the Washington Humane Society), and outlined a system of fines and legal jurisdictions.

Dr. Putnam Jacobi and other medical leaders (including the physiologist Henry Bowdich of Harvard, the surgeon William W. Keen of Jefferson Medical College, and the internist William Osler and the pathologist William H. Welch both of Johns Hopkins) all objected to the bill strenuously. They observed that medical researchers had been singled out from others using animals for scrutiny at the whim of and by persons ignorant of biology, medicine, and physiologic experimentation. Osler fumed at the distorted antivivisection propaganda (see figure 1). The bill did not pass and until the Animal Welfare Act of 1966 (USPC 2131 et seq.), no laws affecting the conduct of animal research were on the federal books.

Since 1900 there has been phenomenal progress in most areas of human life, including food, housing, transportation, communication, and manufacturing and farming. Of the many areas of human endeavor perhaps none has had a greater positive impact than biomedical research. The vocabulary of today's children lacks words common for their grandparents, like tuberculosis, polio, measles, diphtheria, typhoid, cholera, and yellow fever. All alive today owe their existence to triumphs over these and other diseases that on a regular basis culled the population. The triumphs are based on the domination of ignorance by knowledge. There are many dramatic examples of success but to the health care professional and the layman alike few are more stunning than those associated with the improved understanding of the pathogenesis, diagnosis, and treatment of cardiovascular disease.

A summary of discoveries in cardiovascular research up to early 1900 is published elsewhere. An abbreviated list of subsequent advances in the cardiovascular field is given in table 1. There have been dramatic improvements in the diagnosis, prevention, and treatment of cardiovascular ailments. Before 1942 tetralogy of Fallot was an anatomic curiosity providing some insight into the embryogenesis of the heart. The Blalock-Taussig procedure, developed in dogs, gave hope to the otherwise normal children and their families. Recently the development of tissue-type plasminogen activator (t-PA) as a therapeutic thrombolytic agent, again critically evaluated in dogs, has been carried from the laboratory to the bedside. Biotechnology, itself the product of animal research, makes it possible to produce t-PA in appropriate quantities. The domination of ignorance by knowledge has given hope to countless persons who a mere 30 years ago would have died. Estimates of the positive value of the contributions of such discoveries to society or their positive...
value to loved ones and close associates are impossible.

This progress depended on the careful and slow evolution of detailed information. It started with William Harvey before 1628. "I began to think, as it were, that there might be a motion [of the blood] in a circle. . ."  In describing this work, Sir Michael Foster, the father of British physiology, continued, "to that true view of the motion of the blood he [Harvey] was led by a series of steps, each in turn based on the heart as seen in the living animal, or as he himself says 'repeated vivisections'." Harvey undertook his researches at great personal risk of persecution from the church. This human curiosity has been well described by a noted anthropologist: "One of the most important characteristics of the human species has been our desire to acquire knowledge: through the ages this goal has led to remarkable advances in the natural sciences and in technology."

The pioneering work of Harvey on the circulation is the foundation of modern physiology. The painstaking work of scientists and physicians in the late 19th and early 20th centuries laid the way for the explosion of progress after World War II, as summarized table 1. The greatest advances are correlated with the strong public support of biomedical research, particularly through the National Institutes of Health. It has been argued that the public policy of supporting biomedical research has been America's greatest gift to the world, a domination of ignorance by knowledge.

As clearly indicated by table 1, the dog is the hero of the dramatic advances in diagnosis and treatment of cardiovascular disease. On the other hand, Dr. Franklin Loew, Dean of Tufts University School of Veterinary Medicine points out, "there are more dogs and cats (110 million in the United States) than there are people in many other countries. . . . Dogs are America's sacred cows. They block traffic; they defecate in public; we don't eat them for food." It is on this dual role for the dog and other animals that a heated public debate hinges.

Over the past several years there has been an apparently new militant protest to animal experimentation. A number of serious threats and attacks have been perpetrated against scientists, scientific laboratories, and public property. A group calling itself the Animal Liberation Front (ALF) claims responsibility for many of these raids. ALF is a secret organization with close links to a group called People for the Ethical Treatment of Animals (PETA). Materials stolen by ALF from laboratories wind up in the hands of PETA with remarkable rapidity. PETA uses materials out of context to mislead unwitting individuals and media. For one magazine interview, a director of PETA took a
TABLE 1
Selected examples of major advances in cardiology that depended on animal research

<table>
<thead>
<tr>
<th>When initiated or culminated</th>
<th>Medical advance</th>
<th>Species studied</th>
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<tbody>
<tr>
<td>Pre 1900</td>
<td>Management of heart failure</td>
<td>Dogs</td>
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<td></td>
<td>Blood pressure, heart rate</td>
<td>Many species</td>
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<tr>
<td>Early 1900s</td>
<td>Electrocardiography</td>
<td>Dogs</td>
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<td></td>
<td>Cardiac catheterization</td>
<td>Dogs, rabbits, cats</td>
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<td>1920s</td>
<td>Ventilation with open thorax</td>
<td>Dogs</td>
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<tr>
<td>1930s</td>
<td>Transfusion, blood groups and typing</td>
<td>Many species</td>
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<td></td>
<td>Anticoagulants</td>
<td>Cats</td>
</tr>
<tr>
<td></td>
<td>Pump oxygenator</td>
<td>Cats, dogs</td>
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<tr>
<td>1940s</td>
<td>Blue baby operation</td>
<td>Dogs</td>
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<tr>
<td>1950s</td>
<td>Cardiac pacemaker</td>
<td>Dogs</td>
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<td></td>
<td>Floating cardiac catheter</td>
<td>Dogs</td>
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<td></td>
<td>Open heart surgery</td>
<td>Dogs</td>
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<tr>
<td>1960s</td>
<td>Selective coronary angiography</td>
<td>Dogs</td>
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<td></td>
<td>ventriculography</td>
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<td></td>
<td>Defibrillation</td>
<td>Dogs</td>
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<tr>
<td></td>
<td>Coronary collateral circulation</td>
<td>Dogs, pigs, primates</td>
</tr>
<tr>
<td></td>
<td>Coronary bypass</td>
<td>Dogs</td>
</tr>
<tr>
<td></td>
<td>Modern cardiopulmonary resuscitation</td>
<td>Dogs</td>
</tr>
<tr>
<td>1970s</td>
<td>Modern treatment of coronary insufficiency</td>
<td>Dogs</td>
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<tr>
<td></td>
<td>Elective cardiac arrest</td>
<td>Dogs</td>
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<td></td>
<td>Vascular anastomosis</td>
<td>Dogs</td>
</tr>
<tr>
<td></td>
<td>Measures of coronary blood flow in humans</td>
<td>Dogs</td>
</tr>
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<td></td>
<td>Myocardial preservation techniques</td>
<td>Dogs</td>
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<td></td>
<td>Beneficial effects of exercise on the heart (cardiac re-habilitation)</td>
<td>Dogs</td>
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<tr>
<td></td>
<td>Heart transplant</td>
<td>Dogs</td>
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<tr>
<td>1980s</td>
<td>t-PA</td>
<td>Dogs</td>
</tr>
<tr>
<td></td>
<td>Artificial heart</td>
<td>Dogs</td>
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*Modified from Krasney.*

reporter to interview a member of ALF. On national television another director of PETA, who is best known for her statement, "A rat is a pig is a dog is a boy," flatly denied membership in ALF. The materials stolen from laboratories have been used very effectively to publicize PETA and its political programs.

The propaganda and extensive letter-writing campaigns organized by PETA and related organizations have generated considerable support in Congress for legislation to control and restrict animal experimentation. After a 1960s style protest with occupation of buildings of the NIH campus by PETA sympathizers, the Animal Welfare Act of 1966 was amended a third time in December 1985 to incorporate a number of important new restrictions into law. Detailed regulations are still being written, but every biomedical researcher knows the law has changed, although its impact is still not fully apparent. Ignorance dominated knowledge. The biomedical community chose to ignore repeated warning that they were targets of intense scrutiny. Many of the rules mandated by the law of 1985 could place inappropriate persons in control of the research processes through protocol review.

The tactics of terrorism against researchers and public and private laboratories are new and have intimidated researchers in English-speaking countries. Originating in England at about the same time that dogs began to be bred for hunting and for show as pets, several competing groups were founded ostensibly to prevent abuse to beasts of burden and other farm animals. Some active members of the group were influenced by vegetarian philosophy imported from India. French experimental physiology introduced important new facts and concepts into medicine before anesthetics became available. Some members of the dominant Royal Society for the Prevention of Cruelty to Animals (RSPCA) became concerned about "cruelty" in the laboratory, which can be translated to mean "pain," often conjured from the depiction of mechanical apparatus in the scientific literature. These ideas from industrial England were taken up in urban America about a decade later. No enthusiasm could be found for them in rural America, where people were in daily contact with vermin, predators, game, and livestock.

In the early 1860s objects to vivisection in England actually had to go to France to find institutions practicing vivisection. It is ironic that the most offensive of these was a French veterinary school. Middle class citizens with some upper class support from conservative and religious quarters financed printing of pamphlets and other publications that were systematically distributed at places of business and social clubs (see figure 1). The fact that a majority of physiologic and surgical experiments were conducted on anesthetized subjects after anesthesia was introduced did not cause the agitators to correct their propaganda. It was a retired veterinary surgeon with no physiologic experience who wrote the first major attack on animal experimentation.

In the 1870s a series of highly publicized incidents involving insensitive scientists and physicians offended the aesthetics of the English. Subsequently a combination of well-financed skillful propaganda in news media and the effective lobbying of members of Parliament led to the passage of the Cruelty to Animals Act of 1876. Under this law licenses for experiments...
were denied to a number of leading workers, including Sir Thomas Lauder Brunton, who developed nitrates for treatment of angina. In 1896 and again in 1900 bills were introduced into the U.S. Congress to regulate animal experimentation in the District of Columbia, but they also failed.\textsuperscript{1, 20}

It is not entirely clear what motivated attempts to regulate animal experiments in the infancy of the era of biomedical research. It is clear that other social questions such as women’s issues, social climbing, fear of science and scientific discovery, challenges to religious belief, the incredible changes in the social order, the inequitable distribution of wealth, and the translocation that accompanied the industrial revolution all contributed.\textsuperscript{18, 19, 21} A philosophical base was the evolution of animals from the soulless machines of Descartes to the sentient creatures of Jeremy Bentham. An anti-intellectual mood fired by distorted propaganda (see figure 1), effective use of media, and cultivation of strong political allies, all well financed by donations, would have made it difficult to resist a law in the United States much into the 20th century had not the biomedical research paid off in a way that all could appreciate. The powerful benefits of the antitoxin to diphtheria made many skeptics believers in the value of biomedical research.\textsuperscript{22} It turned out to be an excellent practical benefit of biomedical research with which to deal with the political problem of attempted regulation.

For the past 120 years groups of antivivisection activists have attempted to regulate and restrict animal experimentation through legislation at the local, state and national level. Alert and prominent leaders in biomedical research have addressed the issue in several forums. The interactions led to the formulation and endorsement of voluntary rules of conduct for laboratory research.\textsuperscript{23} Awareness of the problem changed the language of scientific reports: animals were “sacrificed” rather than “killed.”\textsuperscript{21} From the very beginning there were animal welfare organizations of many stripes. Mainline organizations like the Humane Society, with some local exceptions, seemed to accept animal research, devoting their energies to policing animal abuse by private individuals and to protecting pets. These organizations have become wealthy through gifts and are targets for takeover by radical animal activists.

Immediately after World War II, the protests of animal welfare groups were still largely targeted to individual institutions. However, the very acts of Congress that led to enlightened increases in biomedical research support through the NIH\textsuperscript{26} and other agencies formed a paradoxical Achilles heel for biomedical research. Animal welfare activists early on realized that reducing sources of support for biomedical research would ultimately terminate research.\textsuperscript{19} Federal support is a focal source that can be attacked efficiently. The Animal Welfare Act of 1966 apparently was enacted by playing on fears that pets would be used in research, although there was no hard evidence at the time that any pets were kidnapped.\textsuperscript{15} (Current evidence is that 80% of pets received by animal shelters are brought for disposal by their owners\textsuperscript{25}. ) The law of 1966 required inspections of animal care facilities at research institutions, of some pet stores, and for commercial exhibitors such as circuses. The inspectors are organized by the Department of Agriculture and the rules include periodic evaluation by private or staff veterinarians.

After the Viet Nam war, there was a sharp rise in activism concerning animals. Up to that time various organizations (often consisting of only a few persons) promoted regulation of animal research on the assumption that the majority of experiments are painful for the subjects. The traditional support of animal welfare was largely supplanted in the public attention by radicals. The stated keys to those organizations, of which PETA and ALF are examples, are two philosophical streams. One espouses animal liberation, which had its origins in the writings of Australian Philosopher Peter Singer.\textsuperscript{26} Singer’s views are influenced by vegetarian thought and are broad in their implication. The use of animals for research, food, hides, and other purposes is likened to racism for which the term “speciesism” has been coined. Another view is that called animal rights.\textsuperscript{27} In this view animals are born with legal rights that traditionally belong to human beings. Establishing a modern philosophical base (over 100 years ago the antivivisectionists bolstered their efforts with philosophical, religious, and “moral” arguments) has been critical to make the movements appear legitimate. These two philosophical views have been scrutinized by professional philosophers who find “animal rights” and “animal liberation” seriously flawed in logic, assumptions, and conclusions (e.g., Cohen\textsuperscript{28}). It is evident that after the hype is cleared away the goals are political. For instance, the first part of an extensive essay on animal liberation is an account of licit and illicit political action for which the author takes credit.\textsuperscript{26} In another, the main result of the philosophy is equated with a “political movement.”\textsuperscript{27}

Other than the principal complaint of cruelty and pain directly to pets or primates, opponents to animal research also suggest various alternatives to animal experiments. Newkirk’s suggestion of human experi-
mentation is out of line for scientific and ethical reasons. A second complaint is duplication of research. To prevent this it is suggested that exhaustive literature searches be conducted. However, it is well known to professionals that biomedical science moves so quickly that direct "grapevine information" is the only way to stay abreast of "hot" fields. A third alternative is tissue culture. In some areas, such as single myocardial cell biophysics, this may be appropriate, but in others, such as the study of dynamics of ventricular contraction, it is inappropriate. Several centers set up to explore such alternatives have closed, primarily because of lack of continuing support from any organization, including those concerned with animal well being. Finally, computer simulations have been suggested as a method of research. Such suggestions are clearly made from ignorance of biology and of computer science. Discussion of a "simple" problem helps to put the issue in perspective: "Even a precise treatment of the condensation of water vapor and the growth of a single droplet to precipitation size is beyond the capability of available computers."

Animal rights and welfare activists have been largely responsible for the legislation under which biomedical research organizations are now compelled to operate. It is also very likely that they had an inordinate input into the drafting of lengthy proposed definitions and regulations that could have become administrative law had not individual biomedical scientists and organizations protested forcefully. A responsibility of health care professionals is to resist these attempts to subvert the public interest and will. The issue of animal experimentation is being evaluated by a number of national committees. Distinguished figures in the biomedical field have attempted to interact directly with persons representing animal welfare organizations. While the reports are still to appear, the heat of the interactions has broken into the popular press. These exchanges differ little from numerous earlier debates conducted on opinion pages of newspapers at earlier times. The arguments between Ms. Stevens, wife of the politically influential long-time director of the Kennedy Center for the Performing Arts in Washington, D.C., and Dr. Michael DeBakey are clearly drawn. They point to the utter impossibility of reaching general understanding with animal welfare activists that is consistent with the knowledge gained by years of education and the priorities of desperate people seeking relief from serious afflictions (see also Woolsey et al.). Ms. Stevens argues that she is qualified to evaluate research by virtue of being the daughter of a scientist, which is like assuming that a person is qualified to fly a jumbo jet by virtue of being a frequent flier.

A provision of the current regulations under which experiments are permitted deserves comment. An institutional committee reviews research protocols that involve animals. The workload on committee members in an active institution is enormous. In spite of this, it is absolutely critical that knowledgeable scientists remain part of the active review process. Members who are required on the committee are a lay person and a veterinarian. The latter's role is critical for several reasons. For instance, the veterinarian reviews the appropriateness of drugs, life support systems, surgical anesthesia, and mode of euthanasia. The report from American Veterinary Medical Association's panel on euthanasia is mandated as guide. The use of this report is appropriate in veterinary practice, but it is clearly inadequate for research. In one example the reference cited as a contraindication to decapitation is clearly incorrect. Yet recommendations based on this incorrect information have interrupted research throughout the country.

What can be done at this stage to prevent the further domination of knowledge by ignorance? Each health care professional and biomedical researcher must insist that high professional and technical standards be maintained in the use and care of laboratory animals. Second, access to research areas, animals, equipment, and records should be kept secure. Third, individual researchers should become actively involved in the affairs of their institutional animal care committees. Committee members need to be supported and to be educated. Present local interactions will have a great impact for the future. Fourth, individual health care professionals can contribute to the support of national and local organizations involving in promoting research (i.e., Foundation for Biomedical Research, 81 Connecticut Ave., N.W., Suite 303, Washington, DC 20006; 202/457-0654) and actively clarify to laymen the role of biomedical research in current prevention, diagnosis, and treatment of illness. Fifth, individuals can act through professional societies and organizations to become informed about animal activists and how to deal with the problems they present. Sixth, local and national professional societies can become strong advocates of biomedical research through support of appropriate organizations and concerted political action. Finally, and most importantly, the public must be constantly reminded that the source of most of the modern medical miracles is biomedical research on animals; it must understand that hope for the future (such as cure for AIDS) rests in biomedical research.
with animals. One way to ensure this would be to add a single line to be read and initialed on informed consent forms such as “I understand that the procedure to which I consent was developed with knowledge from experiments on animals.”

In the final analysis those that suffer most from the political activities of the groups seeking to restrict biomedical research on animals are people who are or will become patients needing help and hope. Dennis Feeney, a paraplegic, has written an excellent article on this topic in which he asks: “Please do not forget those of us who suffer from incurable diseases or disabilities who hope for a cure through research that requires the use of animals.” A major responsibility of all health care professionals, regardless of their chosen specialty, is to ensure that ignorance does not dominate knowledge. That goal requires experiments professionally conducted by professionals on animals in laboratory. Although he was referring to the Cruelty to Animals Act of 1876, Michael Foster’s (who also represented Cambridge University in Parliament) summary of the situation for his worried American colleagues nearly 100 years ago has an eerie and prophetic tone: “The act took birth in England: (1) from the energy of doctrinaires of the upper middle classes . . . who had the time and funds for public agitation, while men of science and doctors had something else to do and hated agitation. (2) Because certain leaders in science and medicine, fearing the strength of the doctrinaires, advised compromise (the compromise has proved one-sided). . . . My advice . . . is, accept no compromise whatsoever; . . . fight against it everywhere, in the newspapers and on the platform and refuse a political vote to a candidate who will not . . . vote against [regulation].” Animal welfare, animal rights, and animal liberation are first and foremost part of a political struggle. The struggle is to determine whether there will be, as Dr. Putnam Jacobi put it, “the domination of knowledge by ignorance” progressively regulating animal experiments out of existence, or whether there will be “the domination of ignorance by knowledge,” which is a trait unique to Homo sapiens, through future experiments that must be on animals.

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